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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/345,761	07/01/99	ISHIGURO	T 054969

EXAMINER	
ART UNIT	PAPER NUMBER
1655	16

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Advisory Action

Application No.	Applicant(s)
09/345,761	Ishiguro, T et al.
Examiner	**Group Art Unit**
CB Wilder	1655

THE PERIOD FOR RESPONSE: [check only a) or b)]

a) ☒ expires 8 months from the mailing date of the final rejection.

b) ☐ expires either three months from the mailing date of the final rejection, or on the mailing date of this Advisory Action, whichever is later. In no event, however, will the statutory period for the response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition, and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally set shortened statutory period for response or as set forth in b) above.

☒ Appellant's Brief is due two months from the date of the Notice of Appeal filed on Jan 10, 2001 (or within any period for response set forth above, whichever is later). See 37 CFR 1.191(d) and 37 CFR 1.192(a).

Applicant's response to the final rejection, filed on Jul 10, 2000 has been considered with the following effect, but is NOT deemed to place the application in condition for allowance:

☒ The proposed amendment(s):

☒ will be entered upon filing of a Notice of Appeal and an Appeal Brief.

☐ will not be entered because:

☐ they raise new issues that would require further consideration and/or search. (See note below).

☐ they raise the issue of new matter. (See note below).

☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.

☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE: _____

☐ Applicant's response has overcome the following rejection(s):

_____

☐ Newly proposed or amended claims _____ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claims.

☒ The affidavit, exhibit or request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See attachment to Advisory Action

☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

☒ For purposes of Appeal, the status of the claims is as follows (see attached written explanation, if any):

Claims allowed: _____

Claims objected to: _____

Claims rejected: 1-20

☐ The proposed drawing correction filed on _____ ☐has ☐has not been approved by the Examiner.

☐ Note the attached Information Disclosure Statement(s), PTO-1449, Paper No(s). _____ .

☐ Other

ATTACHMENT TO ADVISORY ACTION

1. Applicant's amendments filed January 3, 2001 (Paper No. 14) will be entered upon notice of Appeal and an Appeal Brief. Claims 21-23 have been canceled . Claims 1-20 and 29 are pending. The claim rejections under 35 USC. 112 second paragraph are withdrawn in view of Applicant's amendment of the claims. The prior art rejections under 35 U.S.C. 103(a) are maintained for the reasons discussed below.

Previous rejections

2. Applicant traverses the rejection on the following ground: Applicant argues that "Davey et al. neither disclose nor suggest a first single stranded oligo nucleic acid as the reagent (A) according to the present invention". Applicant argues that "both in the method of the present invention and the process of Davey et al., in order to amplify the nucleic acid sequence (a characteristic which distinguishes the target nucleic acid from other nucleic acids, which is referred to as the specific nucleic acid sequence in the present invention) it is necessary that the nucleic acid sequence be at the 5' end of the target RNA". Applicant further argues that "Davey et al. describe an RNA which functions as the first template as containing at its 5' end a sequence which is sufficiently homologous to that which is at the 3' end of the second primer". Applicant states that among naturally occurring RNA molecules, some have indefinite sequences at the 5' end, some have no 5' end due to their circular shape and some do not have a characteristic sequence like the sequence used for determination for the subtype of the hepatitis C virus (HCV) at the 5' end". Applicant argues that

"the specific nucleic acid sequence in such an RNA can not be amplified by the process of Davey et al., without preparing a first template by cutting the RNA so that the first template has the specific nucleic acid sequence at the 5' end". Applicant continues by stating that "Davey et al. says nothing about use of an oligo nucleic acid for the purpose of cutting the target RNA at the 5' end of the specific nucleic acid sequence so that the resulting RNA fragment has the specific nucleic acid sequence located at the 5' end as in the present invention". Applicant further argues that 'in contrast to the Davey et al. method, the use of the oligo nucleic acid as the reagent (A) in the present invention had the advantage that it is based on the specificity of the hybridization between the oligo nucleic acid and the target RNA". Applicant states that "this is not true of the Davey et al. reference".. Applicant further states that "the Davey et al. reference does not disclose anything about detection of the amplified RNA with a fluorescent intercalative dye-labeled DNA whose presence in a reaction solution makes detection of the amplified RNA possible". Applicant points out to the Examiner that "reagent (A) a first oligo nucleic acid) according to the present invention does *not* function as a template, unlike Davey et al., but rather is used to facilitate cutting the single stranded RNA in a sample at the 5' end of the specific nucleic acid sequence to be amplified. Finally, Applicant argues that Davey et al. does not suggest the purpose for using the reagent (A) in the present invention, not to mention the effect of reagent (A) and does not teach or suggest the combined use of the mutually related reagents or teach that the combined use of the reagents realizes more sequence-specific detection of a specific nucleic acid sequence".

2. The arguments filed in Paper No. 14 have been thoroughly reviewed and considered but they are not found persuasive for the reasons that follows: First in response to Applicant's arguments that Davey et al. do not teach or suggest a first oligonucleotide as reagent (A) for the purpose of cutting the target RNA at the 5' end of the specific nucleic acid sequence so that the resulting fragment has the specific nucleic acid sequence located at the 5' end as in the present invention, the Examiner would like to point out to Applicant that the limitations Applicant is arguing are not recited in the claims as written. The courts have established that during patent examination the pending claims must be interpreted as broadly as their terms reasonably allow *(In re Zletz, 893 F.2d321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989))*. In this case, the claims only suggest that the method comprise the reagents (A) through (J) in any combination or order but do not provide any specific function of the claim reagents. In fact, the claimed method do not provide any particular method step but only suggest that reagents (A) through (J) be provided. Therefore it is unclear how the method operates to achieve its goal. Likewise, there is no prescribed or specific function of reagent (A) or an effect of reagent (A) as Applicant argues, therefore in contrast to Applicant's arguments, the claimed reagent (A) is not limited to an enzyme that facilitates cutting of the single-stranded RNA in a sample at the 5' end but could simply function as a template. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. *See In re Van Geuns, 988 f.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).* Finally in response to Applicant's argument that the Davey et al. reference does not disclose anything about the detection of the amplified RNA with a fluorescent intercalative dye-labeled DNA whose presence in the reaction

solution makes detection of the amplified RNA possible, one cannot show non-obviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, the teaching of detection using an fluorescent intercalative dye is provided by the secondary reference of Ishiguro et al.. Motivation for combining the reference of Ishiguro et al. with Davey et al. as discussed in the prior Office Action (Paper No. 11) is provided in the teaching of Ishiguro et al. that performing an amplification process with a fluorescent DNA intercalative dye allows the quantitative detection of RNA over a wide dynamic range. Ishiguro et al. further adds that this system is a powerful tool for the quantification of a starting material with excellent reliability and clinical significance. In view of the foregoing, the rejections under 35 USC 103(a) are maintained.

3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Cynthia Wilder whose telephone number is (703) 305-1680. The examiner can normally be reached on Monday through Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached at (703) 308-1152. The official fax phone number for the Group is (703) 308-4242. The unofficial fax number is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed the Group's receptionist whose telephone number is (703) 308-0196.

Cynthia B. Wilder

Cynthia B. Wilder, Ph.D.

February 8, 2001

W. Gary Jones
Supervisory Patent Examiner
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2/12/01